UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/754,723	01/04/2001	Ole Kirk	3745.234 US	3358

23650 7590 09/08/2004

NOVO NORDISK PHARMACEUTICALS, INC
100 COLLEGE ROAD WEST
PRINCETON, NJ 08540

EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/754,723	KIRK, OLE	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08295913.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 6-14-04 has been entered into the record. Claims 15-32 are pending and under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter is withdrawn in view of Applicants pointing to the specification by page and line number where support in the specification can be found.

The rejection of claims 15-20 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of Applicants pointing to the specification by page and line number where support in the specification can be found.

The rejection of claims 15 and 19 under 35 U.S.C. 102(b) as being anticipated by Knick et al , in "Bachmann, Lotz, Mchnert (Hsrg)." Insulin/Sulfonylharnstoff. Symp. Munchen 1986, pages 98-106; Karger, Basel 1988) is withdrawn in view of the amendment of the claims to recite "insulinotropic".

Knick et al teach the use of the combination therapy of Metformin and Insulin for the treatment of 16 Type II diabetic patients were the insulin was injected and the Metformin taken in tablet form (see bottom page 99 and top of page 103). Insulin is applied under the provision of derivative or analogue of GLP because insulin has a single amino acid in common with GLP and as such the

combination of oral metformin and injected insulin as administered to Type II diabetics meets the limitations of the claim.

Rejections Maintained

Claims 15-20 and new claims 21-32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Buckley et al (WO 91/11457) in view and Gutniak et al (Diabetologia, 33(suppl):A73, Abstract 246, 1990) of Ramachandran et al (Diabete Metabolisme, 13(2):140-141, 1987) Del Prato et al (The American Journal of Medicine, 90(suppl 6A):6A-77S, 1991) and Parker et al (Diabetes, Volume 40, Suppl 1, Abstract 847) is maintained for all reasons made of record and those herein.

Applicants' arguments have been carefully considered but are not persuasive. Applicants argue no reasonable expectation of success. This is not persuasive, both drugs were known and suggested for use to treat Type 2 diabetes. Since both drugs are effective in vivo to treat an aspect of diabetes, the combination would reasonable be expected to be effective. Applicants argue that it is impossible to predict what the combined effect of the two different drugs would be and combination therapy is an unpredictable art. This is not persuasive, drugs are routinely combined in the art. The drugs as combined treat the identical disease absent factual evidence to the contrary. Applicants appear to argue that absent an actual reduction to practice, one could not predict the ability of the combination to treat Type 2 diabetes. Applicants appear here to argue that their own specification is not enabled. Their own specification does not in fact reduce the combination to practice and relies on constructive reduction to practice by filing a patent application. The examiner maintains that the art is as enabling as Applicants own specification at the time of filing. Applicants own specification is devoid of any teaching that the combination is effective to treat Type II diabetes as claimed.

Therefore if the art is so unpredictable, then Applicants specification is also not enabled for the claimed combination of drugs. The examiner does not concede that the art is not enabling. The dosages and routes of treatment for the individual drugs were know in the art. Applicants own specification relies upon these dosages to enable the specification, therefore the art is as enabling as Applicants specification. Applicants argue combinations of drugs not know to the art at the time of filing and not in the field of diabetes and as such is not persuasive. Applicants argue that certain drugs are contraindicated with other drugs and have adverse warnings. This again is not persuasive, there is and was at the time the invention was made no adverse warning regarding the combination as set forth in the rejection and therefore the asserted "potential" for adverse side effects is seen as a negative teaching and does not teach away from combining drugs known to treat the same disease. Applicants argue that there is not certainty that any combination of drugs will or will not work. This is simply not so. Each of the drugs in the combination have been established in the art to treat Type 2 diabetes. One would expect the combination to work to treat Type 2 diabetes. There is no teachings in the art at the time of filing that indicate that the combination would not work and the art is as enabling as the specification. Applicants argue specific contraindications for diabetic patients having certain other problems. Adverse drug effects with respect to the entire genus of Type 2 diabetes patients is not a patentability issue, unless the entire patient population has an adverse condition. Further, adverse drug effects are not the purview of the Patent Granting Process, but rather a concern for the regulatory agency that governs approval of drugs. Applicants argue combinations of Avandia™ are unpredictable. This is not persuasive, because the combination is not over Avandia™. Applicants argue that absent clinical trials, one can not predict which result harmful or beneficial will be obtained. This is not persuasive, again both drugs are taught by the art for the

treatment of Type 2 diabetes and it is prima facie obvious to combine such. Clinical trials are not required for patentability, mere reasonable expectation of success. Because the drugs individually are taught for use for treatment of type 2 diabetes, it logically and necessarily follows that the combination of drugs would be useful for the treatment of type 2 diabetes. Reasonable expectation of success is predicated on the teachings of the individual drugs for effective therapy and correlation of the in vitro results with the in vivo results for each drug. The expectation of success is reasonable and is not required to be absolutely predictable. This combination is not an obvious to try, it is common sense. Applicants allegations of unpredictability of combination of drugs is not persuasive. Applicants again argue that the individual teachings of each of the references and not the references as combined. These arguments are again not persuasive, for all the reasons already made of record. Applicants again hindsight reconstruction and no suggestion in the references to combine GLP-1 with SU or metformin. This again is not persuasive. *In re* Fine, 837 F.2d 1071, 1075, 5U.S.P.Q.2d 1959 (Fed. Cir. 1988) states that under section 103 a *prima facie* case of obviousness can be established by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art can lead the individual to combine the references. See also *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). As previously set forth Rachmadan et al teach the combination of glibenclamide and metformin for the treatment of Type 2 diabetes. The combination as recited provides for addition GLP-1 to the type 2 diabetes treatment modality, and the art as combined demonstrates that the *in vitro* effects of GLP-1 are reproducible *in vivo*. As such, the motivation is clearly set forth in the art as cited. Reasonable expectation of similar results is provided by the cited art that indicates GLP-1 provides for additional secretion of insulin from cells *in vitro* and would be expected to display the same effect *in vivo* because

Gutniak et al teach that the insulinotropic effect (i.e. increasing insulin secretion) are reproducible *in vivo*. The combination of agents is *prima facie* obvious over the art for reasons made of record and the idea of combining them logically flows from the art as each being used in combination or alone for treatment of Type 2 diabetes.

The rejection is maintained.

New Rejections Based on Amendment

Claims 22 and 30-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims now recite the use of any single function peptide that has the activity of insulinotropic. The specification fails to provide conception by way of written description of this genus in the specification as filed. The genus as now claimed includes other insulinotropic peptides such as glucose-dependent insulinotropic peptide (GIP), secretin or hormones such as CCK. This broad genus does not conception by way of written description in the specification as filed and is not supported by the described subgenus of GLP-1 related peptides and analogues thereof. This issue was similarly explored by the courts in *In re East and Harmon* (CCPA) 181 USPQ 716 (May 9, 1994) in which claims of a reissue application are drawn to new matter since they broadly recite genus of "carrier particles" which is not disclosed in original patent, which discloses only subgenus of "magnetic carrier particles" and species of "iron, ferrites, nickel, and cobalt" carrier particles.

Claims 15-21, 23 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claims 15-20, 21 and 23-27, the claims are rendered confusing because it apparently recites GLP-1(7-36)amide twice in the claim (see second line after second recitation of "or"). It is unclear if Applicants are intending here to claim analogues of GLP-1(7-36) amide. If Applicants intend to claim analogues of GLP-1(7-36)amide then the claims should be amended to recite the members in the alternative such as X, Y or Z. If Applicants do not intend to claim analogues of GLP-1(7-36)amide, then the repetitive subject matter should be deleted. Further, as to claims 23 or 24, the claims recite conventional Markush language "selected from the group consisting of" however do not recite a closed group using the phrase "and" and as such the metes and bounds of the group are indefinite. Applicants can choose the format (i) "wherein the insulinotropic peptide is X,Y or Z" or (ii) "wherein the insulinotropic peptide is selected from the group consisting of X, Y and Z". The mixture of the two renders the metes and bounds of the alternatives in the group indefinite. Clarification of the claims is requested.

Status of Claims

All claims stand rejected.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-F 6:30 am - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patricia A. Duffy

Primary Examiner